CANCER ASSESSMENT OF THE LIBBY AMPHIBOLE
PROJECT PLAN: **13 Sept 2007**
Updated – Feb 2008

Objective: Conduct a Cancer Health Assessment of sufficient quality and detail to support the derivation of an inhalation unit risk (IUR)for the Libby Amphibole, as data are available.

Overview:
A recent mortality update of the NIOSH Libby, MT worker cohort is expected to provide sufficient information for derivation of a unit risk. The cancer assessment will include a discussion of 1) mineral fiber toxicity in general, 2) animal bioassays with tremolite, LA or other amphiboles, 3) relevant mechanistic and *in vitro* studies and 4) epidemiologic and health studies as support for the cancer descriptor and quantitative assessment. Additional data will be incorporated as it becomes available (e.g. mortality analysis of Marysville, OH Cohort, NHEERL LA animal research). Project will be conducted per the Integrated Risk Information System (IRIS) SOPs for Health Assessments and in accordance with applicable US EPA Guidance.

Project Description:

Background/Objectives:

The town of Libby, MT and related mining and processing facilities for vermiculite ore, were contaminated with a unique amphibole fiber material originally identified as tremolite asbestos. EPA's decision to take action at this site is based on health assessments using the EPA inhalation unit risk for asbestos, as recommended (NCEA 1999). Although EPA has been conducting removal and clean-up activities to reduce community exposures, Region 8 must produce a baseline risk assessment to support Superfund clean-up activities and the final Record of Decision. In order to reduce uncertainty and provide the best scientific basis for Agency decision making, it is preferable that this baseline risk assessment consider the potency of the particular fibrous amphibole material found in vermiculite mined in Libby, MT.

EPA has been working in Libby since 1999 when an Emergency Response Team was sent to investigate local concern and news articles about asbestos-contaminated vermiculite. Since that time, EPA has been working closely with the community to clean up contamination and reduce risks to human health. The mine processing facilities and the town itself were contaminated with vermiculite containing the Libby Amphibole. However, final clean-up standards have not been developed.

Epidemiologic studies of the workers in Libby, MT demonstrate increased plural anomalies, asbestosis, lung cancer and mesothelioma. Earlier reports have been able to develop quantitative dose-response relationships for lung cancer but not mesothelioma

incidence. Residents in Libby who were not workers for the mining and processing operations also exhibit health effects consistent with exposure to fibrous amphiboles, including pleural anomalies and some asbestosis (ATSDR publications). Therefore, developing a health assessment for the Libby amphibole is an important public health action.

Risk Assessment Process:

The Libby Amphibole (LA) Cancer Assessment will provide information on the carcinogenic hazard potential of LA and quantitative estimates of risk inhalation exposure. The information includes a weight-of-evidence judgment of the likelihood that the agent is a human carcinogen and the conditions under which the carcinogenic effects may be expressed. In general, quantitative risk estimates for IRIS are derived from the application of a low-dose extrapolation procedure, and route-specific risk values are presented. The "oral slope factor" is an upper bound on the estimate of risk per mg/kg-day of oral exposure. Similarly, a "unit risk" is an upper bound on the estimate of risk per unit of concentration, either per μg/L drinking water or per $\mu g/m^3$ air breathed. To date, the majority of health and toxicological information available, addresses the inhalation pathway. Therefore, it is expected this effort will focus on development of an inhalation unit risk

Development of this hazard identification and dose-response assessment for Libby Amphibole mineral fibers will follow the general guidelines for risk assessment as set forth by the National Research Council (1983). EPA guidelines that were used in the development of this assessment include the following: *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a), *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* (U.S. EPA, 2005b), *Guidelines for the Health Risk Assessment of Chemical Mixtures* (U.S. EPA, 1986a), *Recommendations for and Documentation of Biological Values for Use in Risk Assessment* (U.S. EPA, 1988), (proposed) *Interim Policy for Particle Size and Limit Concentration Issues in Inhalation Toxicity* (U.S. EPA, 1994a), *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (U.S. EPA, 1994b), *Use of the Benchmark Dose Approach in Health Risk Assessment* (U.S. EPA, 1995), *Science Policy Council Handbook: Peer Review* (U.S. EPA, 1998b, 2000a, 2005c), *Science Policy Council Handbook: Risk Characterization* (U.S. EPA, 2000b), *Benchmark Dose Technical Guidance Document* (U.S. EPA, 2000c), and *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (U.S. EPA, 2000d).

Literature Search:

The literature search strategy employed for this compound will be based on the CASRNs for asbestos, amosite, actinolite and tremolite, and relevant key words (Libby amphibole, tremolite, asbestos, mineral fiber, winchite, richtorite). Any pertinent scientific information submitted by the public to the IRIS Submission Desk will also be considered in the development of this document. The relevant literature is current through June, 2007, and will be updated during the course of the project.

Document Development:

This cancer assessment will follow the general outline for IRIS, revised to focus on the carcinogenicity of the Libby Amphibole. Document text, including review and summaries of relevant literature will be written by NCEA scientists and all available data will be considered in this review. Main topics covered will include:

- Geology and mineralogy of Libby Amphibole
- Overview of mineral fiber toxicity
- Critical review of available animal and *in vitro* studies
- Critical review of available human studies
- Hazard identification and Mode of Action discussions
- Quantitative risk estimates

NIOSH has recently updated their database on the Libby worker cohort, publishing a mortality analysis (Sullivan, 2007). The data reported in this publication and detailed discussions with the primary investigator (PI), indicate this dataset may now support a dose-response analysis which could provide the basis of an Inhalation Unit Risk (IUR) specific to the Libby Amphibole material. Modeling and statistical analysis of epidemiologic data will be done in collaboration with NIOSH.

Document Review and Revision:

Internal EPA Review Processes:
Once a draft document is completed an internal peer consultation will be conducted. The draft document will be sent to selected experts throughout the Agency for a review. Additionally, the document will be presented to NCEA management and staff scientists, allowing for a broad base of input from NCEA scientists.

Agency Review is a more formal process where all IRIS assessments are reviewed by a panel of Agency experts, representing Program offices, the Regional offices and stakeholders across the Agency. This review will include technical as well as programmatic input. Comments from the Agency reviewers will be addressed and the document prepared for External Review.

External Document Review:
The first step of external review is the Office of Management and Budget (OMB) at the White House. OMB may at their discretion distribute the document to other Federal Agencies for review and comment. Once all comments are received and resolved the document will be prepared for expert peer consultation.

The Libby amphibole Cancer Assessment will undergo Expert Peer Review after interagency review. An expert panel may be convened by the EPA's Science Advisory Board, which is establishing a standing committee to review asbestos related documents.

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Task	Start Date	End Date
Initiate Assessment		18 Jan 2007
Project Planning Literature Search Assemble project team Establish IAG with NIOSH	18 Jan 2007	24 Aug 2007
Document Development Literature reviews Hazard Identification Carcinogenicity Assessment Quantitative modeling	27 Aug 2007	16 June 2008
Internal EPA Review Processes and document revision Internal Peer Consultation EPA IRIS Agency Review	30 June 2008	15 Dec 2008
External review Process OMB / Interagency review External Peer consultation (EPA SAB)	1 Feb 2009	2 Nov 2009
Final Document Revisions and Posting to the IRIS database	2 Nov 2009	17 May 2010